Attorney's Docket No.: 17105-026001 / 0062 Applicant: J. Chen **Amendment & Response**

Serial No. : 09/760.362 Filed

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January 12, 2001

AMENDMENTS TO THE CLAIMS

Claims 1-6, 11, 12, 16-24, 36 and 38-56 are presently pending in this application. Claim 46 is amended herein and claims 50-56 are added herein. This listing of claims replaces all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (Previously presented) A method to treat neovascular disease of the eye, comprising:

administering a conjugate comprising a photosensitizing compound conjugated to a targeting moiety that selectively binds to abnormal endothelium that lines or composes neovascular target tissue in the eye;

allowing sufficient time to permit the non-specifically bound conjugate to clear from non-target tissue; and

illuminating the neovascular tissue with light including a wavelength corresponding at least in part with the characteristic light absorption wavelength of the photosensitizing compound for a period of time sufficient to activate the photosensitizing compound; wherein:

a combination of an intensity of light used for the step of illuminating and a duration of illumination is selected to produce a total fluence of irradiation such that the neovascular target tissue is destroyed and the non-target tissue through which the light passes remains undamaged.

- 2. (Previously presented) The method of claim 1, wherein the light is noncoherent light.
- (Previously presented) The method of claim 1, wherein the light is 3. coherent light.
- 4. (Previously presented) The method of claim 1, wherein the neovascular tissue is present in retina, choroid or both.
- 5. (Original) The method of claim 1, wherein the treated neovascular disease is diabetic retinopathy.
- (Original) The method of claim 1, wherein the treated neovascular disease is macular degeneration.

Claims 7 - 10 (Cancelled)

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11. (Previously presented) The method of claim 1, wherein the targeting moiety is a first member of a binding pair and wherein a second member of the binding pair is selected from the group consisting of a receptor present on abnormal endothelium; a ligand bindable to a receptor present on abnormal endothelium; an antigen present on abnormal endothelium; and an antibody bindable to an antigen present on abnormal endothelium.

12. (Previously presented) The method of claim 11, wherein the conjugate is incorporated into a liposomal preparation.

Claims 13 -15 (Cancelled)

- 16. (Previously presented) The method of claim 1, wherein the targeting moiety is a bi-specific antibody construct that further comprises both a ligand component and a receptor component.
- 17. (Previously presented) The method of claim 16, wherein the conjugate is incorporated into a liposomal preparation.
- 18. (Previously presented) The method of claim 1, wherein the photosensitized neovascular tissue is illuminated for at least 4 minutes.
- 19. (Previously presented) The method of claim 1, wherein the photosensitized neovascular tissue is illuminated for at least 20 minutes.
- 20. (Previously presented) The method of claim 1, wherein the photosensitized neovascular tissue is illuminated for at least 1 hour.
- 21. (Previously presented) The method of claim 1, wherein the photosensitized neovascular tissue is illuminated for at least 24 hours.
- 22. (Previously presented) The method of claim 1, wherein the neovascular tissue is treated with a total fluence of light irradiation from between about 240 J/cm² to about 900 J/cm².
- 23. (Previously presented) The method of claim 2, wherein the non-coherent light source is a light emitting diode.
- 24. (Previously presented) The method of claim 2, wherein the non-coherent light source is ambient light.

Claims 25 - 35 (Cancelled)

36. (Original) A method of instructing a person to treat neovascular disease of the eye, comprising instructing a person to conduct a method according to claim 1.

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> 37. (Cancelled)

38. (Previously presented) The method of claim 1, wherein the targeting moiety is an antibody that binds to a VEGF receptor.

- (Previously presented) The method of claim 1, wherein the targeting 39. moiety is VEGF.
- 40. (Previously presented) The method of claim 1, wherein the targeting moiety is a VEGF receptor.
- 41. (Previously presented) The method of claim 1, wherein the photosensitizing compound is a chlorin.
- 42. (Previously presented) The method of claim 1, wherein the photosensitizing compound is selected from the group consisting of chlorins. bacteriochlorophylls, phthalocyanines, porphyrins, purpurins, merocyanines, psoralens, benzoporphyrin derivatives (BPD), porfimer sodium, δ-aminolevulinic acid protoporphyrin, indocyanine green (ICG), methylene blue, toluidine blue, texaphyrins, pyropheophorbide compounds, bacteriochlorophyll derivatives, alkyl ether analogs of chlorins, verteporfin and benzoporphyrin derivatives.
- 43. (Previously presented) The method of claim 1, wherein the photosensitizing compound is verteporfin or texaphyrin.
- 44. (Previously presented) The method of claim 1, wherein the photosensitizing compound is indocyanine green.
- 45. (Previously presented) The method of claim 1, wherein a combination of an intensity of light of less than 500 mW/cm² and a duration of illumination of at least 4 minutes is selected to produce a total fluence of light irradiation from between about 30 J/cm² to about 25,000 J/cm².
- 46. (Amended herein) A method to treat neovascular disease of the eye, comprising:

administering a targeted photosensitizing compound that selectively binds to abnormal endothelium that lines or composes neovascular tissue in the eye;

allowing sufficient time to permit the non-specifically bound conjugate to clear from non-target tissue; and

illuminating the neovascular tissue with light for a period of time sufficient to activate the photosensitizing compound thereby causing damage to neovascular tissue, but without impairing or destroying other tissue, wherein

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a combination of an intensity of light used for the step of illuminating and a duration of illumination is selected to produce a total fluence of irradiation such that the neovascular tissue is destroyed and the non-target tissue through which the light passes remains undamaged, wherein

the neovascular tissue is treated with a total fluence of light irradiation from between about 240 J/cm² to about 900 J/cm².

- 47. (Previously presented) The method of claim 46, wherein the light is non-coherent light.
- 48. (Previously presented) The method of claim 47, wherein the noncoherent light source is a light emitting diode.
- 49. (Previously presented) The method of claim 47, wherein the noncoherent light source is ambient light.
- (New) The method of claim 46, wherein the photosensitizing 50. compound is incorporated into a liposome.
- (New) The method of claim 50, wherein a ligand, receptor or bispecific construct is incorporated in or attached to the liposome.
- 52. (New) A method to treat neovascular disease of the eye, comprising: administering a conjugate comprising a photosensitizing compound selected from among chlorins, bacteriochlorophylls, phthalocyanines, porphyrins, purpurins, merocyanines, psoralens, porfimer sodium, δ-aminolevulinic acid protoporphyrin, indocyanine green (ICG), methylene blue, toluidine blue, texaphyrins, pyropheophorbide compounds, and verteporfin conjugated to a targeting moiety selected from among VEGF ligand, VEGF receptor, antibody or antibody fragment that binds to VEGF receptor, a complete or functional bindable fragment of human antibody L19, ανβ3 integrin, the extra-domain B of fibronectin or carcinoembryonic antigen (CEA);

allowing sufficient time to permit the non-specifically bound conjugate to clear from non-target tissue; and

illuminating the neovascular tissue with light including a wavelength corresponding at least in part with the characteristic light absorption wavelength of the photosensitizing compound for a period of time sufficient to activate the photosensitizing compound; wherein:

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a combination of an intensity of light used for the step of illuminating and a duration of illumination is selected to produce a total fluence of irradiation such that the neovascular target tissue is destroyed and the non-target tissue through which the light passes remains undamaged; and

the neovascular tissue is treated with a total fluence of light irradiation from between about 240 J/cm² to about 900 J/cm².

- 53. (New) The method of claim 50, wherein the light is non-coherent light.
- (New) The method of claim 50, wherein the light is coherent light. 54.
- 55. (New) The method of claim 50, wherein the neovascular tissue is present in retina, choroid or both.
- (New) The method of claim 50, wherein the photosensitized 56. neovascular tissue is illuminated for a time interval of between 4 minutes and 72 hours.